## REMARKS

Claims 1-20 are pending. By this amendment, claims 8, 11 and 20 are amended to more precisely recite the features of the claims. No new matter is introduced. Support for the amendments may be found at least at page 11, lines 2-3 of the specification. Reconsideration and allowance of the claims in view of the above amendments and the remarks that follow are respectfully requested.

***Rejection Under 35 U.S.C. § 102***

Claim 20 stands rejected under 35 U.S.C. § 102(a) as being anticipated by Nakamura et al. for reasons stated on page 3 of the Office Action. Applicants respectfully traverse the rejection.

For anticipation under 35 U.S.C. §102, the reference "must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." (MPEP §706.02, IV. Distinction between 35 U.S.C. 102 and 103, page 700-21). The Federal Circuit has held that prior art is anticipatory only if every element of the claimed invention is disclosed in a single item of prior art in the form literally defined in the claim *(Jamesbury Corp. v. Litton Indus. Products*, 756 F.2d 1556, (Fed. Cir. 1985); *Atlas Powder Co. v. DuPont;* 750 F.2d 1569, (Fed. Cir. 1984); *American Hospital Suppl v. Travenol Labs*, 745 F.2d 1 (Fed. Cir. 1984).

Claim 20, as amended, recites a method for monitoring the effectiveness of treatment of a subject with an agent that inhibits telomerase activity. The telomerase activity is determined using the method of claim 1.

Nakamura generally describes the deduction of telomerase activity in human liver cancer cells by a histone deacetylase inhibitor. Nakamura does not teach or suggest detecting telomerase activity using "a reaction tube comprising: a first reaction mixture comprising a first primer and nucleoside triphosphates; a second reaction mixture comprising a second primer and a DNA polymerase; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube," as recited in claim 1.

Accordingly, Applicants respectfully submit that Nakamura does not anticipate claim 20 because it fails to teach every aspect of the claimed invention. Withdrawal of the rejection to claim 20 under 35 USC 102(a) over Nakamura is respectfully requested.

***Claim Rejections Under 35 U.S.C. §103***

Claims 1-6, 8-13 and 15 stand rejected under 35 U.S.C. § 103(a) over Harley et al. (hereinafter "Harley") in view of Elmore et al. (hereinafter "Elmore") for reasons stated on pages 4-12 of the Office Action. Claims 7 and 14 stand rejected under 35 U.S.C. § 103(a) over Harley in view of Elmore and further in view of Choo et al. (hereinafter "Choo") for reasons stated on pages 12-13 of the Office Action. Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness ... the prior art reference (or references when combined) must teach or suggest all of the claim limitations. *In re Vaeck,* 947 F.2d 488 (Fed. Cir. 1991) and *MPEP* § 2142.

Independent Claim 1 of the instant application is directed to a method for detecting and quantifying telomerase activity in a biological sample, the method comprising the steps of: adding the biological sample to a reaction tube comprising: a first reaction mixture comprising a first primer and nucleoside triphosphates; a second reaction mixture comprising a second primer and a DNA polymerase; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube; incubating the biological sample with the first reaction mixture under conditions suitable for a telomerase to produce an extension product from the first primer, said extension product having a 3' end; admixing the extension product with the second reaction mixture by melting the wax layer; amplifying the extension product using a real-time polymerase chain reaction under conditions that allow the detection of telomerase activity from a single 293T cell; and quantifying the amplified extension product using a control template.

Harley generally describes a method for detecting and quantifying telomerase activity. Harley does not teach or suggest the step of "adding the biological sample to a reaction tube comprising: a first reaction mixture comprising a first primer and nucleoside triphosphates; a second reaction mixture comprising a second primer and a DNA polymerase; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube," as recited in claim 1.

Elmore and Choo do not cure the deficiency of Harley. Elmore generally describes a method of quantitative analysis of telomerase activity in breast cancer specimens. Choo generally describes a method wherein the control template has a nucleotide sequence recited in SEQ ID NO: 2. Elmore and Choo, however, fail to teach or suggest the step of "adding the biological sample to a reaction tube comprising: a first reaction mixture comprising a first primer and nucleoside triphosphates; a second reaction mixture comprising a second primer

and a DNA polymerase; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube," as recited in claim 1.

The Examiner admits that Harley does not teach a method wherein both the polymerase and second primer are separated from the first reaction mixture by a wax layer. The Examiner, however, alleges that "the purpose of the wax barrier is to separate the telomerase extension reaction from the amplification reaction ... there is no functional reason or obvious advantage to have or not have one of the reagents present in the telomerase mixture" (the Office Action, page 12).

Applicants respectfully submit that biotechnology is generally considered an unpredictable art. It is well known to one skilled in the art that the presence of additional primers in a reaction mixture may lead to unexpected results, especially in a situation where two reactions (i.e., the telomerase-mediated primer extension and PCR amplification) are carried out sequentially in the same tube. Therefore, it would not be obvious to one skilled in the art to place the second primer and the DNA polymerase under the wax layer in view of Harley's teachings. Accordingly, Applicants respectfully submit that Harley, Elmore and Choo, individually or in combination, do not render claim 1 obvious.

Independent claim 8, as amended, is directed to a method for detecting and quantifying telomerase activity in a sample cell, the method comprising the steps of: suspending the sample cell in a cell suspension; passing the cell suspension through a needle at least once; introducing into a sample cell a first primer and nucleoside triphosphates; incubating the sample cell under conditions suitable for a telomerase to produce an extension product from the first primer; amplifying the extension product using real-time polymerase chain reaction; and quantifying the amplified extension product using a control template.

Harley, Elmore and Choo do not teach or suggest the steps of "suspending the sample cell in a cell suspension" and "passing the cell suspension through a needle at least once," as recited in claim 8. The Examiner alleges that Harley teaches the step of passing cells through a needle because Harley mentions fine needle aspirates used to biopsy tumor tissue. Applicants respectfully submit that the purpose of passing cell suspension through a needle in the instant invention is to break cell aggregates and to form a more uniformed cell suspension. A fine needle biopsy is used to take out a small piece of tissue from a target organ. It does not involve a cell suspension and does not teach or suggest using a cell suspension. Therefore, Applicants respectfully submit that Harley, Elmore and Choo, individually or in combination, do not render claim 8 obvious. Applicants further submit that

claims 2-7 and 9-14 are patentable because they depend from one of claim 1 and 8, and because they recite additional patentable subject matter.

For example, Harley, Elmore and Choo do not teach or suggest the step of "elongating the extended product at the 3' end by one of polyadenylation and ligation," as recited in claim 6. The Examiner alleges that Harley teaches this step and cites col. 9, lines 37-52 of Harley as support. Applicants respectfully submit that the cited paragraph refers to primer extension (i.e., elongation from the primer), but not elongation from an extended product. Harley also fails to mention anything about elongating an extended product by polyadenylation.

Independent claim 15 of the instant invention is directed to a method for detecting and quantifying telomerase activity in a biological sample, the method comprising the steps of: adding the biological sample to a reaction tube comprising: a first reaction mixture comprising a first primer and nucleoside triphosphates; a second reaction mixture comprising a second primer and a DNA polymerase; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube; incubating the biological sample with the first reaction mixture under conditions suitable for a telomerase to produce an extension product from the first primer, said extension product; elongating the extended product at a 3' end by one of polyadenylation and ligation; admixing the extension product with the second reaction mixture by melting the wax layer; amplifying the extension product using a real-time polymerase chain reaction under conditions that allow the detection of telomerase activity from a single 293T cell; and quantifying the amplified extension product using a control template, wherein the second primer comprises a nucleotide sequence that is complementary to the nucleotide sequence at a 3' end of the elongated extension product.

As discussed earlier, Harley, Elmore and Choo, individually or in combination, fail to teach or suggest a reaction tube comprising "a first reaction mixture comprising a first primer and nucleoside triphosphates; a second reaction mixture comprising a second primer and a DNA polymerase; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube" and the step of "elongating the extended product at a 3' end by one of polyadenylation and ligation," as recited in claim 15. Accordingly, claim 15 is patentable over Harley, Elmore and Choo. Withdrawal of rejections under 35 USC 103(a) is respectfully requested.

In view of the above amendments and remarks, Applicant respectfully submits that the application is in condition for allowance. Prompt examination and allowance are respectfully requested.

Should the Examiner believe that anything further is desired in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,

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